NAMING THE AIDS VIRUS

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Summary

Several names have been used for the human retrovirus recently identified as the causative agent of the acquired immune deficiency syndrome (AIDS). During the past year, a subcommittee of the International Committee on the Taxonomy of Viruses has considered many candidates for a widely acceptable name for the AIDS virus, in the light of new information about this virus and modern genetic approaches to virus classification. The many issues — scientific, social, and political — that bear on this decision are reviewed, and the formal proposal of the subcommittee is presented in a Postscript.

Between April 1983 and August 1984, three research groups in three locales three thousand miles apart reported the isolation of viruses advanced as candidates for the causative agent of the acquired immunodeficiency syndrome (AIDS) (1-3). Although these viruses were each called different names by the laboratories that reported them, the many isolates obtained by these groups now appear to form a very closely-related virus group within the large and well-studied class known as retroviruses (4). By the end of 1984, it was apparent that both the scientific community and the public would be better served by a single name for the causative agent of AIDS, but it was much less clear what that name should be or what criteria should be applied to decide.

Since March, 1985, I have chaired a committee composed of thirteen well-known retrovirologists from four countries, attempting to find a single acceptable name for this important new group of human retroviruses, ~~while addressing each other only by letter or telephone~~. This duty has fallen to me because I chair a standing subcommittee, known as the Retrovirus Study Group, which is empowered to rule on matters of retroviral nomenclature and classification under the aegis of a larger group known as the International Committee on the Taxonomy of Viruses. We were summoned to action on this occasion ~~when I began to receive~~ by calls and letters from virologists close to and distant from the experimental activity, asking that some neutral group offer a solution to what had become an intractably confusing and at times even bitter contentious issue.

The normal workings of ~~this group, as you might imagine,~~ are sporadic, often pedantic, and of little concern to the general public, albeit useful to those who must work with and talk about viruses. In the case of the AIDS virus, however, our activities have attracted extraordinary attention and curiosity.

Why has there been so much interest in the resolution of a problem which would appear to have no immediate relevance to the serious issues in the AIDS crisis---controlling the spread of this virus and treating its victims? Some perceive, wrongly in my view, that our final recommendation will form a verdict upon contested issues of priority of discovery, issues that could influence patent rights, the awarding of major prizes, patriotic sentiments, and financial gain. Others have seen our deliberations as a battle between Robert Gallo and Luc Montagnier, both members of the Committee and leaders of the two most highly publicized groups to isolate AIDS retroviruses; this is certainly an oversimplified view of the proceedings. For many who follow the AIDS problem closely as experimental scientists, health care workers, or public-spirited citizens, the issue may simply be one of having a single, convenient, and generally accepted name for the virus that causes the disease. And for an appreciable number of scientists, the task has a higher purpose, eloquently expressed by Stephen Jay Gould (5):

"...taxonomies are not neutral hatracks for the pristine facts of nature. They are theories that create and reflect the deep structure of science and human culture. A taxonomy is not just a ploy for convenient arrangement, but a hypothetical statement about the nature of things."

In fact, the issue before us has not been taxonomy per se, but nomenclature; we have attempted to settle upon what is usually called the common or species name for a virus or collection of very similar viruses. Since such names are in daily use by the working virologist, much ink and some blood has been spilled over them; the forces that influence decisions about them are as various as the forces that influence the naming of a baby, a book, a bridge, or a city.

Scientific principles, political realities, aesthetics, convention, and justice must all be served in the process of finding the species name for a virus. Many questions had to be considered for each suggestion ~~during the protracted process~~: Is the proposed name consistent with scientific facts and with ~~its~~ the virus' tentative classification? Is there anything objectionable about the name that would prevent its being used? Have those credited with discovery been accorded their rights to contribute to the process of naming? Does the name distinguish the virus from those it does not resemble? Is the name readily remembered? Is the name likely to create confusion in the future if and when other viruses are isolated? Does the name conform to existing conventions for naming viruses of this general type?

Before discussing specific names proposed for the AIDS virus, I must briefly introduce a debate that has been raging among namers of viruses for the past few years. The definition of an animal species is based upon the ability to mate productively; membership in a species is granted to those animals that can interbreed with other members. Since viruses do not have sex in the conventional sense, grouping of viruses that are so closely related as to be accorded a common name was often based upon in the past any conveniently measured biological or biochemical property---such as virus shape, or immune reactivity, or presence of a certain enzyme in the virus particle.

With the application of new genetic and molecular techniques to the study of viruses, however, it has become possible to define virus groups in a fashion analogous to that used for animals, in a way that is likely to come closer to establishing true evolutionary relationships among viruses (5). In this new view, it is possible to assess which viruses are so closely related genetically that they could exchange genes without loss of viability, in the manner of animals that can generate viable offspring by the intermingling of

their genes. Such viruses properly constitute a species and can usually be clearly distinguished from those that are genetically disparate, regardless of other similarities.

In the context of the AIDS viruses, for example, it was apparent by the time our deliberations began that the available isolates were sufficiently closely related to be considered members of the same virus species. The questions, in large part, were whether and how they should be distinguished from human retroviruses that appeared to belong to other species.

What names did we have to consider? Several names were already in use. Most prominent among these were lymphadenopathy virus (LAV), human T cell lymphotropic virus-III (HTLV-III), AIDS-associated retrovirus (ARV), two hybrid names (HTLV-III/LAV and LAV/HTLV-III), and a name often used by the press (the AIDS virus). In short order, many more names, about fifty when all permutations are counted, were suggested by committee members, consultants, and other correspondants.

How could we decide among these many candidates? When confronted by confusion, it is sometimes useful to ~~take a conservative position, and~~ consider what has worked well in the past. Retroviruses form a large group of agents united by a distinctive property: they carry their genes in the form of ribonucleic acid (RNA) and convert them to deoxyribonucleic acid (DNA) after infection, reversing the usual flow of information in nature from DNA to RNA. However, despite this unifying feature, retroviruses are also manifestly diverse: they are found in many different animal hosts, cause several different types of disease, and frequently appear to be only marginally related when the substance of their genes is carefully examined (6). This complexity has generated a need to group isolates in a rational manner that emphasizes biological boundaries.

Traditional retroviral nomenclature has worked well in this regard. The convention has been to name viruses according to the host species of origin and the prominent pathology associated with the prototypic isolate of a single type; two examples of such names are "feline leukemia virus" and "mouse mammary tumor virus." Individual isolates belonging to a single species are further distinguished by prefixes or suffixes (numbers, letters, or [in earlier times] names of discoverers), as in "Rauscher murine leukemia virus" or human "T cell leukemia virus-2."

Many of us have favored staying close to these traditional rules, but there were obviously other considerations as well. In particular, the rights of discoverers needed to be respected, but it was clear from outset that we could not reach a consensus about eminent domain. It thus seemed prudent to set as an objective the best possible name, to include all claimants in the proceedings, and to hope that all parties would find some solution acceptable.

If we were to adopt a traditional name for the AIDS retrovirus, we needed to consider a particularly troubling issue: whether names that included the term "AIDS", such as "human AIDS virus" or "human AIDS-lymphadenopathy virus," were likely to be psychologically damaging in the clinic in view of the lethality of the disease and the social stigmas attached to the prevalent routes of virus transmission. To explore this issue, we asked over fifty clinicians who had worked with AIDS patients for their opinions. The large number who responded showed geniune and intelligent interest in the choice of names, but they were almost exactly divided over the issue of whether to exclude "AIDS" from the name. Some took the position that patients would soon be as fearful of any term that denoted the agent of AIDS as they would be about a term that was explicit, a phenomenon our committee has referred to as "the evanescence of euphemism." Others felt strongly that it

was easier to explain the difference between infection by the virus and the disease induced in a minority of infected people, if the virus had a name with less perjorative potential.

There was general agreement among our membership that the latter view should prevail, if only because strict adherence to simplicity and convention was not important enough to outweigh the misfortune of even a rare patient suffering needlessly from the report of an antibody test. Moreover, it was possible to consider use of terms that denote the principal pathological consequences of infection---e.g. "immunodeficiency" or "immunosuppression"---thereby avoiding the name of the disease, yet conforming to standard nomenclature.

The many names suggested for the AIDS virus raised other taxonomic possibilities. Some encouraged the use of host cell affinities as a basis for the name, a view already in wide circulation through the use of "human T cell lymphotropic virus" and endorsed by other suggestions, such as "human T4 virus" which names the cellular receptor that determines whether the virus can enter a cell. (This approach is discussed more fully below.) Another possibility was raised by experimental evidence linking the AIDS virus with a handful of animal retroviruses that produce disease slowly and are hence known as lentiviruses, one of the three large subgroups of retroviruses (7). However, enthusiasm for "human lentivirus-1" was dampened by the still weakly defined characteristics of this class and by the inappropriateness of using as a species name a name normally applied to a collection of diverse virus species. Others suggested defusing the political, clinical, and genetic issues through the use of a sequential numbering system, in which the AIDS virus would become human retrovirus-3. However, colorless names of this type can be difficult to connect with the right virus, especially when the list

becomes lengthy; the approach does not respect the genetic basis of virus speciation, since human retroviruses from different species would have names that differ only by number; and attempts to impose similar systems upon other virus groups, such as human herpesviruses, have not always been successful.

From a pragmatic perspective, we had to consider the already widespread use of the term human T cell lymphotropic virus-III (HTLV-III) and to ask whether it was too firmly entrenched to be displaced by a new name. This tactical question, however, was accompanied by closely linked to the theoretical issue of how modern virologists view the world, and how they recreate it for their students through the choice of names, because the term HTLV-III presents a direct challenge to the genetic basis of virus speciation.

Proponents of HTLV-III wish to group it with HTLV-I and -II---viruses orginally called human T cell leukemia viruses, but proposed to be renamed as T cell lymphotropic viruses---based upon a long list of common features (8). However, the most prominent of these similarities appear superficial and deceptive when closely examined. Thus, though both virus types have strong predilections for infecting the T4 subset of thymus-derived lymphocytes, the mechanisms determining that preference are fundamentally different for the leukemia viruses and the AIDS virus; the two groups of viruses use different host cell receptors to gain entry into the lymphocytes, and, as a consequence, they also differ with regard to other cell types they can infect. Second, though the leukemia and AIDS viruses are pathogenic for man, they cause dramatically different types of pathology, resulting on the one hand from inappropriate proliferation of infected cells and on the other from toxicity and death of infected cells. Third, despite several similarities in size of the proteins found in leukemia and AIDS virus particles, the sequences of the building blocks (amino acids) of these proteins are now known to be as

different as the sequences for any two ostensibly unrelated retroviruses. Finally, though both types of viruses exhibit relatively unusual mechanisms for improving the efficiency with which they produce the proteins encoded by their genes, on close inspection the mechanisms appear to be largely unrelated (9).

The explanation of these fundamental differences is immediately apparent when the viral chromosomes (known as genomes) are compared (10). Though the genomes of the AIDS and leukemia viruses share features that are common to all retroviruses ~~from all animals~~---symmetrical units at the ends ~~that~~ govern gene expression and ~~the~~ a basic layout of genes for the proteins found in virus particles---wherever they can differ, they do. Most obviously, the order of the components of the genome differs, so that the sequence of nucleotides is no more similar for these two groups than for any two members of the diverse family of retroviruses. But important subtleties are also evident: the manner in which the major genes are juxtaposed assigns the viruses to different classes, and the position and nature of other genes ~~other than those that encode proteins for the virus particles~~ are entirely unrelated.

If an evolutionary tree is established for retroviruses by comparing the order of amino acids in the protein most characteristic of retroviruses, the enzyme that converts RNA to DNA, it is apparent that the AIDS virus is most closely related to the sheep lentivirus, called visna, whereas the human T cell leukemia viruses are in another limb of the tree, more closely related to other oncogenic viruses, leukemia and sarcoma viruses of various animals, particularly the bovine leukemia virus (7). To those who believe in the application of genetic principles to virus nomenclature, it is apparent that a superficial resemblance in host cell tropism should not be used to impose a species designation upon viruses that are highly divergent according to rigorous criteria.

Through a series of memoranda and polls that sought a consensus on these issues, we narrowed the choices to a few and ~~unfortunately~~ identified a name approved by a resounding majority, but not by acclamation. (That name and the letter officially proposing it to the scientific community ~~is~~ presented in the Postscript.) The issue that remains is a practical one: can we bring this name into common use? Or will we simply have added an academic suggestion, albeit one enshrined in the official logs of an international agency, to the list of names already used?

Colleagues sometimes ask why we should care about this issue, with convictions that go beyond the usual manifestations of good scientific citizenship. During our deliberations, at least two components of our commitment have emerged. As proponents of the disciplines of virology and genetics, we want them to operate in a way that seems to us and to students we train scientifically sound. Moreover, we would like the public view of our science to be one that acknowledges the reality of disagreement, but one that also admires the willingness of intellectual combattants to compromise for advancement of our shared purpose. A prolonged battle over the issue of a name for the AIDS virus is more than trivial, because it may come---some might say it has come---to symbolize certain excesses of character for which scientists are often criticized. This seems particularly unfortunate in view of the truly extraordinary accomplishments that have been made in a very short time by the laboratories involved in the debate. A generally accepted recommendation for a name for this virus could help restore to the public whatever faith has been been lost through this issue during the confusion of the past two years.

Postscript

During the first week of May, 1986, the following letter from our Subcommittee appeared in the journals Nature and Science. Two members of our group, Myron Essex and Robert Gallo, declined to sign the agreement.

To the Editor:

The undersigned are members of a subcommittee empowered by the International Committee on the Taxonomy of Viruses to propose an appropriate name for the retrovirus isolates recently implicated as the causative agents of the acquired immune deficiency syndrome (AIDS). Adoption of an internationally-acceptable name for this group of viruses has become an important issue because of the widespread interest in AIDS and its origins and because of the multiplicity of names currently in use. Thus the several isolates of what are now evidently closely related members of the same virus group have been called lymphadenopathy associated virus (LAV), human T cell lymphotropic virus type III (HTLV-III), immunodeficiency associated virus (IDAV), and AIDS-associated retrovirus (ARV). At present, two compound names (HTLV-III/LAV and LAV/HTLV-III) are also used in scientific publications, and the colloquial name, the AIDS virus, is often used by the press.

We are writing to propose that the AIDS retroviruses be officially designated as the human immunodeficiency viruses, to be known in abbreviated form as HIV.

We have considered several issues that bear upon this proposal. (i) The name conforms to common nomenclature for retroviruses, beginning with the host species ("human"), ending with "virus," and containing a word that denotes a major (though not the only) pathogenetic property of the prototypic members of

the group ("immunodeficiency"). ("Feline leukemia virus" and "mouse mammary tumor virus" are two well-known examples of such names for retrovirus species.) (ii) Though the name clearly connects the viruses to the disease with which the virus group is associated, it does not incorporate the term "AIDS", which many clinicians urged us to avoid. (iii) The name is readily distinguished from all existing names for this group of viruses and has been chosen without regard to priority of discovery. (iv) The name is sufficiently distinct from the names of other retroviruses to imply an independent virus species, a group of isolates that can presumably exchange genetic information readily with each other but not with members of other known retrovirus species. These other species include the human T cell leukemia viruses (e.g., HTLV-1 and -2), which will continue to be named according to a convention adopted by several leading investigators in September, 1983. (Though roman numerals are often used to indicate the type of HTLV, arabic numbers were originally prescribed in the agreement and are thus used here.) (v) Retroviruses isolated from subhuman primates and found to be genetically related and biologically similar to HIV's should be designated as immunodeficiency viruses of the appropriate host species (e.g., simian immunodeficiency virus [SIV] or African green monkey immunodeficiency virus [AGMIV]). (vi) Because HIV isolates are numerous and display considerable genetic heterogeneity, particularly in the <u>env</u> gene, it will be necessary for each laboratory to assign subspecies designations to their isolates. We recommend that each laboratory adopt a code with geographically informative letters and sequential numbers to identify their isolates (e.g., the 42nd isolate at the University of Chicago could be described as HIV [CHI-42]). Initially, the existing, well-characterized isolates, such as LAV-1, HTLV-IIIB, or ARV-2, should be identified as such in publications to ease the

transition to a unified nomenclature. (vii) Any future isolates of human retroviruses with clear but limited relationship to isolates of HIV (e.g., more than 20% but less than 50% nucleic acid sequence identity) should not be called HIV unless there are compelling biological and structural similarities to existing members of the group.

We hope that this proposal will be adopted rapidly by the research community working with the viruses.

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